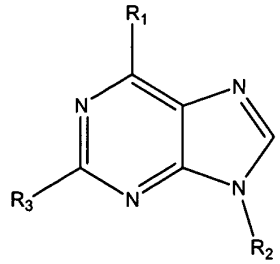
ABSTRACT OF THE DISCLOSURE

02 Disclosed are novel compounds that are inhibitors of CDK2 and IκB-α cell cycle kinases that are useful for treating various disease states, including proliferative diseases such as cancer and restenosis.

IN THE CLAIMS:

Please amend the claims as follows:

03 48. (twice amended) A compound having the formula:



wherein:

R_1 is -X-R_1'; in which R_1' is lower alkyl, substituted lower alkyl, [cycloheteroalkyl, substituted cycloheteroalkyl], aryl, substituted aryl, [aralkyl, substituted aralkyl, hetaryl, substituted hetaryl, and heteroalkyl] or heterocycle, and X is -NH- or -SO_2-;

R_2 is lower alkyl optionally substituted with one, two or three groups selected from hydroxy, lower alkoxy, and halogen[, mercapto, alkylthio, amino, amido, carboxy, cyano, aryloxy, alkenyl, alkynyl, or acyl;

aryl, heteroaryl, arylalkyl or heteroarylalkyl where the ring portion of each is optionally substituted with one, two or three groups selected from lower alkyl, alkoxy, halogen,

mercapto, alkylthio, ethynyl, amino, amido, carboxy, hydroxy, aryl, aryloxy, heteroaryl, nitro, or cyano;

cycloalkyl optionally substituted with one, two or three groups selected from lower alkyl, alkoxy, halogen, thiol, ethynyl, alkylthio, aryl, aryloxy, heteroaryl, nitro, or cyano; or heterocyclyl]; and

R_3 is [halogen, hydroxy, mercapto, alkoxy, alkylthio, lower alkyl, or] $-NR_4R_5$; in which R_4 and R_5 independently are hydrogen or lower alkyl optionally substituted with one, two or three groups selected from hydroxy, lower alkoxy, halogen, amino, [mercapto, alkylthio, amido,] or carboxyl, [cyano, aryloxy, or acyl; or

aryl, arylalkyl, heteroaryl, heteroarylalkyl, or cycloalkyl where the ring portion of each is optionally substituted with one, two or three groups selected from lower alkyl, lower alkoxy, halogen, mercapto, alkylthiol, ethynyl, amino, amido, carboxyl, hydroxy, aryl, aryloxy, heteroaryl, nitro, or cyano;]

with the proviso that:

(1) when R_1 is benzyl or phenylethyl, X is -NH-, and R_3 is NR_4R_5, in which R_4 is hydrogen and R_5 is lower alkyl of C_{1-4} substituted by hydroxy or amino, R_2 is not [lower alkyl of C_{1-4}] methyl or ethyl; [and with the proviso that];

(2) R_1 cannot be cycloalkyl or endo-2-norbornyl when R_3 is halogen, hydroxy, or alkoxy;

(3) R_2 and R_3 cannot both be lower alkyl;[and with the proviso that];

(4) when R_1' is optionally substituted alkyl, the optional alkyl substitution is not heteroaryl;

(5) when R_3 is 2-hydroxyethylamino and R_2 is methyl, R_1-X is not 3-methyl-2-butenylamino, benzylamino, or m-hydroxybenzyl-amino,

when R_3 is 2-hydroxyethylamino and R_2 is isopropyl, R_1-X is not benzylamino, m-hydroxybenzylamino, or 3-methylbutylamino;

when R_3 is 2-hydroxyethylamino and R_2 is 2-hydroxyethyl, R_1 -X is not benzylamino and

when R_3 is selected from the group consisting of 2-methyl-2-hydroxy propylamino and 2 dimethylaminoethylamino and R_2 is methyl, then R_1-X is not benzylamino;

or an acid addition salt[s] or [and] cationic salt[s] thereof.

50. (Once amended) The compound of claim 49, wherein R_1' is lower alkyl, substituted lower alkyl, aryl, substituted aryl, or heterocycle [, aralkyl, substituted aralkyl, hetaryl, or substituted hetaryl,].

Please cancel claims 51 and 52 from the application without prejudice.

53. (Twice amended) The compound of claim [52] 50, wherein R_4 and R_5 independently are hydrogen or lower alkyl substituted with hydroxy or amino.

54. (once amended) The compound of claim 53, wherein R_4 [and] is hydrogen and R_5 [are] is [both] lower alkyl substituted with amino.

55. (Twice amended) The compound of claim 54, wherein [R_4 and] R_5 [are both] is 2-aminoethyl.

58. (Twice amended) The compound of claim 57, wherein R_1' is 4-chlorobenzyl, 4-methoxybenzyl, pyridin-3-ylmethyl, or cyclopropylmethyl.

59. (Twice amended) The compound of claim [55] 53, wherein R_4 and R_5 are [both] independently hydrogen or lower alkyl substituted with hydroxy.

Please cancel claims 63 and 64 from the application without prejudice.

65. (Twice amended) The compound of claim 49, wherein R_1' is lower alkyl, [substituted lower alkyl], cycloalkyl, or substituted cycloalkyl, [heterocyclyl, or substituted heterocyclyl,] R_2 is lower alkyl, and R_3 is $-NR_4R_5$, in which R_4 and R_5 independently are hydrogen or lower alkyl substituted with hydroxy or amino.

68. (Twice amended) A method of inhibiting [treating a disease state in a mammal that is alleviable by treatment with] a cell cycle kinase characterized as CDK2 [inhibitor], comprising administering to a mammal in need thereof a therapeutically effective dose of a compound of claim 48.

Please cancel claim 69 from the specification without prejudice.

70. (Once amended) The method of claim [69] 68, wherein the inhibition of CDK-2 kinase treats a proliferative disease where pathogenesis involves [the disease state is characterized by] abnormal cell proliferation.

71. (Once amended) The method of claim 70, wherein the proliferative disease [state] is rheumatoid arthritis, lupus, diabetes, multiple sclerosis, cancer, restenosis, [graft-host disease] host-vs-graft disease, or gout.

72. (Once amended) The method of claim 70, wherein the proliferative disease [state] is cancer.

73. (Once amended) The method of claim 70, wherein the proliferative disease [state] is restenosis.

Please cancel claims 74 and 75 from the application without prejudice.

Please add the following new claims 77-79 to the application:

77. (New) The compound of claim 59, wherein R_4 is hydrogen and R_5 is 2-hydroxyethyl.

78. (New) The compound of claim 77, wherein R_2 is isopropyl.

79. (New) The compound of claim 78, wherein R_1' is 4-phenylbenzyl, 4-bromobenzyl, 4-bromophenyl, quinolin-3-yl, quinolin-5-yl, quinolin-6-yl, or quinolin-8-yl.